

pausal hormone therapy (HT) use and the risk of breast cancer among women with a benign lesion, hyperplasia with atypia, or carcinoma *in situ* detected. During follow-up, 274 women with a benign lesion, 34 women with hyperplasia with atypia and 118 women with carcinoma *in situ* were diagnosed with invasive breast cancer. They observed an increased risk of breast cancer associated with use of menopausal hormone therapy for women with a benign or premalignant lesion. Alcohol consumption and tobacco smoking showed increased risk of breast cancer among women with a benign lesion. The authors did not give detailed information about the association between risk factors and invasive breast cancer subtypes. We evaluated the associations between several hormonal and non-hormonal risk factors and molecular subtypes of invasive breast cancer [3]. This cross-sectional study consisted of 1884 invasive female invasive breast cancer cases. We found that reproductive and hormonal characteristics (breastfeeding, parity, age at first full-term birth, hormone replacement therapy) were associated with luminal subtype, compared to nonluminal breast cancer, consistent with previous studies. Obesity and overweight increased the risk of triple negative subtype, particularly in premenopausal women. Older age and use of hormone replacement therapy were related to the risk of HER-2 overexpressing breast cancer. Likewise, Pizzato and colleagues [4] compared selected risk factors with breast cancer subtypes, using a case-case approach in 1321 invasive breast cancers. This case-only study showed that triple negative, compared to luminal A, was negatively associated with higher breast density (BD), while it was positively associated with positive family history of breast cancer, higher education and late age at menarche. Fur-

thermore, this study suggested that luminal BH+(ER+and/or PR+, HER2+), compared to luminal A, was positively associated with higher BD, whereas it was negatively associated with parity. Two clinical studies suggest a significant heterogeneity between breast cancer risk factors and tumor subtypes. This issue merits further investigation.

References

1. Altundag K. Association between common risk factors and molecular subtypes of breast cancer: Still debatable issue? *JBUON* 2020;25:2530.
2. Lilleborge M, Falk RS, Sørli T et al. Can breast cancer be stopped? Modifiable risk factors of breast cancer among women with a prior benign or premalignant lesion. *Int J Cancer* 2021 May 14. doi: 10.1002/ijc.33680. Epub ahead of print.
3. Turkoz FP, Solak M, Petekkaya I et al. Association between common risk factors and molecular subtypes in breast cancer patients. *Breast* 2013;22:344-50.
4. Pizzato M, Carioli G, Rosso S, Zanetti R, La Vecchia C. The impact of selected risk factors among breast cancer molecular subtypes: a case-only study. *Breast Cancer Res Treat* 2020;184:213-20.

Kadri Altundag

MKA Breast Cancer Clinic, Tepe Prime, Cankaya, 06800 Ankara, Turkey.

*Corresponding author: Kadri Altundag, MD.
Email: altundag66@yahoo.com*

The place of Omalizumab in the treatment of Carboplatin hypersensitivity

Dear Editor,

Carboplatin (CP) is a second generation platinum derivative commonly used in oncology practice. Common side effects are nausea, vomiting and myelosuppression associated with dose. In addition, more specific toxicities, such as hypersensitivity reactions, can be observed in CP. CP, which is used in malignant diseases such as lung, testis and ovarian cancer, has been reported to cause hypersensitivity reaction in 0.5-25% of the patients [1,2].

CP-induced hypersensitivity reaction is often mediated by IgE. Drug antigens bind to high affinity IgE receptors in mast cells and/or basophils to release inflammatory mediators [3-5]. Studies have shown that reactions to CP develop more often after the 6th cycle and the risk of reactions increases rapidly after the 7th and 8th cycles [4]. These reactions can be observed in seconds, but usually occur 30 min after the infusion has started [4,5].

It is known that premedication and / or desensitization methods by reducing the infusion rate in patients with CP-induced hypersensitivity reactions have not always been successful in tolerating the drug. The effectiveness of alternative chemotherapy regimens is also often limited due

to tumor sensitivity/insensitivity, so drug exchange is not readily possible. This may be an important cause of morbidity and mortality for patients. In recent years, anti-IgE treatment (Omalizumab), which is one of the desensitization methods, has started to be tried.

Omalizumab is a DNA-derived, recombinant humanized immunoglobulin G1κ monoclonal antibody that selectively binds to human IgE. It reduces the amount of free IgE and IgE FcεRI required for activation of mast cells and basophils (3,5). Desensitization with Omalizumab, an anti-IgE that has been shown to be safe and efficacious, has been shown in case reports to improve quality of life and possibly survival, since it allows patients to use chemotherapy agents (3). However, there is no sufficient literature information on how much Omalizumab treatment can treat hypersensitivity reactions.

In conclusion, hypersensitivity reactions caused by CP limit its use because of their potential to cause more severe reactions and even death in the next application. CP-induced hypersensitive reactions may help in the treatment of patients who fail Omalizumab's standard desensitization protocols. However, randomized clinical trials are needed to evaluate the efficacy, safety and response to treatment.

References

1. Chung SJ, Kang SY, Kang RY et al. A new non-dilution rapid desensitization protocol successfully applied to all-grade platinum hypersensitivity. *Cancer Chemother Pharmacol* 2018;82:777-85.
2. Gadducci A, Tana R, Teti G, Zanca G, Fanucchi A, Genazzani AR. Analysis of the pattern of hypersensitivity reactions in patients receiving carboplatin retreatment for recurrent ovarian cancer. *Int J Gynecol Cancer* 2008;18:615-20.
3. Ojaimi S, Harnett PR, Fulcher DA. Successful carboplatin desensitization by using omalizumab and paradoxical diminution of total IgE levels. *J Allergy Clin Immunol Pract* 2014;2:105-6.
4. Sliesoraitis S, Chikhale PJ. Carboplatin hypersensitivity. *Int J Gynecol Cancer*, 2005;1581:13-18.
5. Iwamoto T, Hirai H, Yamaguchi N et al. Carboplatin-induced severe hypersensitivity reaction: role of IgE-dependent basophil activation and FcεRI. *Cancer Sci* 2014;105:1472-9.

Yasemin Benderli Cihan

Kayseri Education and Research Hospital, Dept of Radiation Oncology, Kayseri, Turkey.

*Corresponding author: Yasemin Benderli Cihan, MD.
Email: cihany@ercyies.edu.tr*

Taxane use for breast cancer-related lymphoedema risk

Dear Editor,

The association of taxanes with the development of lymphedema in breast cancer patients was reported previously [1]. Martínez-Jaimez and colleagues in their article [2] identified the risk factors for lymphedema following axillary lymph node dissection (ALND) in a European sample and proposed a lymphoedema prediction model for this population. They reported that the factor contributing most to the risk of lymphoedema was the level of lymph node dissection, and the only patient-related factor in the prediction model was body mass index (BMI). The authors suggested that the main risk factors for lymphoedema following breast cancer treatment are the type of surgery, the woman's BMI, adjuvant chemotherapy and postoperative complications. The authors did not give detailed information about chemotherapy schedules. The association of taxanes with the development of peripheral edema was evaluated previously. Taxanes may cause systemic disruption, which could have a longer-term effect on lymphatic function leading to lymphedema in breast cancer patients. Furthermore, Cariate and colleagues [3] in their hypothesis-generating study investigated risk factors for lymphedema with a specific focus on the potential impact of chemotherapy. They found that patients who received adjuvant taxanes were nearly three times more likely to develop lymphedema than patients

who had no chemotherapy. In conclusion, adjuvant or neo-adjuvant taxane use might be considered one of the main risk factors for the risk of lymphedema. This issue merits further investigation.

References

1. Sisman H, Sahin B, Duman BB, Tanriverdi G. Nurse-assisted education and exercise decrease the prevalence and morbidity of lymphedema following breast cancer surgery. *JBUON* 2012;17:565-9.
2. Martínez-Jaimez P, Armora Verdú M, Forero CG et al. Breast cancer-related lymphoedema: Risk factors and prediction model. *J Adv Nurs* 2021 Aug 7. doi: 10.1111/jan.15005. Epub ahead of print.
3. Cariati M, Bains SK, Grootendorst MR et al. Adjuvant taxanes and the development of breast cancer-related arm lymphoedema. *Br J Surg* 2015;102:1071-8.

Kadri Altundag

MKA Breast Cancer Clinic, Tepe Prime, Cankaya, 06800 Ankara, Turkey.

*Corresponding author: Kadri Altundag, MD.
Email: altundag66@yahoo.com*

Preference of trastuzumab emtansine as a second or third line treatment in patients with human epidermal growth factor receptor 2 positive metastatic breast cancer refractory to trastuzumab and pertuzumab

Dear Editor,

Trastuzumab-emtansine (T-DM1), a novel drug developed for the treatment of HER2-positive breast cancer, is a human epidermal growth factor receptor (HER2) targeted

antibody drug conjugate, composed of trastuzumab, a stable thioether linker, and the potent cytotoxic agent DM1 (derivative of maytansine). The phase III randomized trial EMILIA has shown that T-DM1 provided objective tumor responses and significantly improved progression-free survival